(FILE 'HOME' ENTERED AT 15:38:45 ON 25 MAR 2003)

FILE 'MEDLINE, CANCERLIT, BIOSIS, EMBASE, CAPLUS, BIOTECHDS' ENTERED AT 15:51:35 ON 25 MAR 2003

L1	26077	S MICROPARTICLE OR NANOPARTICLE
L2	810719	S LIPID OR LIPOSOME
L3	89014	S ENCAPSULA?
L4	117	S L3 AND L2 AND L1
L5	87	DUP REM L4 (30 DUPLICATES REMOVED)
L6	244	S FUSOGENIC LIPOSOM?
L7	1	S L6 AND NAN?

L5 ANSWER 80 OF 87 CAPLUS COPYRIGHT 2003 ACS
AN 1994:613000 CAPLUS
DN 121:213000
TI Condensed-phase **encapsulated microparticle** composition for drug delivery and diagnostic applications
IN Fernandez, Julio M.; Knudson, Mark B.
PA Mayo Foundation for Medical Education and Research, USA
SO PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9417786	A1	19940818	WO 1994-US1924	19940210
	W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, UZ, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2155648	AA	19940818	CA 1994-2155648	19940210
	AU 9462479	A1	19940829	AU 1994-62479	19940210
	AU 676543	B2	19970313		
	EP 684812	A1	19951206	EP 1994-909762	19940210
	EP 684812	B1	19980121		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 08509956	T2	19961022	JP 1994-518397	19940210
	AT 162397	E	19980215	AT 1994-909762	19940210
	ES 2114184	T3	19980516	ES 1994-909762	19940210
	US 5654006	A	19970805	US 1994-250464	19940527
PRAI	US 1993-17681		19930212		
	WO 1994-US1924		19940210		

AB The title microparticles (size 0.05-5 .mu.m), which rapidly release an active agent on exposure to a selected target pH, temp., or ligand, are composed of (1) an external **lipid** bilayer membrane which allows influx of cations when exposed to the selected target condition, (2) **encapsulated** within the **lipid** membrane, a condensed-phase **microparticle** composed of a matrix of crosslinked polyionic polymer filaments, which is capable of decondensing to an expanded state when multivalent counterions also present in the matrix are replaced by monovalent counterions, and (3) the compd. to be released, entrapped in the **microparticle** matrix. Localized disruption of the **lipid** membrane and influx of monovalent counterions cause rapid swelling of the polymer matrix and release of the active compd. The **microparticle** matrix may be of comb-polymer glycoprotein filaments which may be sulfated, sulfonated, carboxylated, or phosphorylated. For diagnostic assays, the **lipid** membrane may contain surface-bound anti-ligand mols. which bind to a ligand analyte, and the entrapped compd. may be a detectable reporter mol. An improved procedure is given for isolation of mast cell secretory granules for use in the title applications.

L5 ANSWER 72 OF 87 CAPLUS COPYRIGHT 2003 ACS
AN 1996:401728 CAPLUS
DN 125:67764
TI Targeted delivery via biodegradable polymers
IN Roth, Laurence A.; Herman, Stephen Jack
PA Focal, Inc., USA
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9611671	A1	19960425	WO 1995-US14103	19951011
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2202511	AA	19960425	CA 1995-2202511	19951011
	AU 9539720	A1	19960506	AU 1995-39720	19951011
	AU 700903	B2	19990114		
	EP 785774	A1	19970730	EP 1995-937688	19951011
	EP 785774	B1	20010131		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 10509696	T2	19980922	JP 1995-513488	19951011
	EP 1004293	A2	20000531	EP 1999-202631	19951011
	EP 1004293	A3	20011004		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	AT 198979	E	20010215	AT 1995-937688	19951011
	ES 2155534	T3	20010516	ES 1995-937688	19951011
	US 5879713	A	19990309	US 1997-787647	19970123
	AU 9923614	A1	19990527	AU 1999-23614	19990401
	AU 726472	B2	20001109		
PRAI	US 1994-322092	A	19941012		
	AU 1995-39720	A3	19951011		
	EP 1995-937688	A3	19951011		
	WO 1995-US14103	W	19951011		

AB Delivery of bioactive mols. such as nucleic acid mols. encoding a protein can be enhanced by immobilization of the bioactive mol. in a polymeric material adjacent to the cells where delivery is desired, where the bioactive mol. is **encapsulated** in a vehicle such as liposomes which facilitates transfer of the bioactive mols. into the targeted tissue. Targeting of the bioactive mols. can also be achieved by selection of an **encapsulating** medium of an appropriate size whereby the medium serves to deliver the mols. to a particular target. For example, **encapsulation** of nucleic acid mols. or biol. active proteins within biodegradable, biocompatible polymeric microparticles which are appropriately sized to infiltrate, but remain trapped within, the capillary beds and alveoli of the lungs can be used for targeted delivery to these regions following administration to a patient by infusion or injection. Thus, expression vector pRSVLUC, contg. firefly luciferase cDNA, was dissolved in a 10% soln. of gelling prepolymer having a PEG core with .apprx.5 lactate residues at each end, capped by acrylate groups. This soln., which also contained eosin Y as photoinitiator, was incorporated into pos. charged liposomes contg. the cationic **lipid** analog, 1,2-dioleoyloxy-3-(trimethylammonium)propane. The liposomes were introduced into the rat carotid artery in vivo and gelated by illumination with green light. After 3 days, gene expression was detected in the artery.

L5 ANSWER 66 OF 87 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 97136393 EMBASE
DN 1997136393
TI Peptide-loaded solid **lipid** nanoparticles (SLN): Influence of production parameters.
AU Almeida A.J.; Runge S.; Muller R.H.
CS A.J. Almeida, Unid. Ciencias e Tecnol. Farmaceut., Faculdade de Farmacia, Universidade de Lisboa, Av. das Forcas Armadas, 1600 Lisboa, Portugal
SO International Journal of Pharmaceutics, (1997) 149/2 (255-265).
Refs: 28
ISSN: 0378-5173 CODEN: IJPHDE
PUI S 0378-5173(97)04885-0
CY Netherlands
DT Journal; Article
FS 037 Drug Literature Index
039 Pharmacy
LA English
SL English
AB Solid **lipid** nanoparticles (SLN) are an alternative to particulate carriers made of biodegradable polyesters. The SLN have been sought as vehicles for drug molecules, and their production often uses physiological lipids or **lipid** molecules with an history of safe use in human medicine. However, little has been studied regarding the incorporation of peptides into SLN. This report describes the first studies on the incorporation of lysozyme, as a model peptide, in SLN. Previous to **nanoparticle** preparation, lysozyme was solubilised, until saturation, into the melted **lipid** phase. Production was carried out by a cold homogenisation process. The entrapment efficiency was dependent on the initial solubility of the peptide in the **lipid** phase of the final preparation. The influence of formulation parameters (e.g. type of **lipid**, time of exposure to different temperatures, pressure and the number of homogenisation cycles) on the integrity and activity of the enzyme, was also assessed. The lysozyme molecule remained intact throughout the process without losing its activity, as shown by sodium dodecyl sulphate-polyacrylamide gel electrophoresis and the rate of lysis of Micrococcus lysolideikticus, respectively. This study shows that some proteins are able to endure the harsh procedures of formulation by high pressure homogenisation, making possible the use of SLN as antigen carriers for vaccine delivery.

L5 ANSWER 59 OF 87 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 1998160228 EMBASE
TI DNA-polycation nanospheres as non-viral gene delivery vehicles.
AU Leong K.W.; Mao H.-Q.; Truong-Le V.L.; Roy K.; Walsh S.M.; August J.T.
CS K.W. Leong, Department of Biomedical Engineering, Johns Hopkins University, 726 Ross, Baltimore, MD 21205, United States.
kleong@bme.jhu.edu
SO Journal of Controlled Release, (30 Apr 1998) 53/1-3 (183-193).
Refs: 26
ISSN: 0168-3659 CODEN: JCREEC
PUI S 0168-3659(97)00252-6
CY Netherlands
DT Journal; Conference Article
FS 022 Human Genetics
037 Drug Literature Index
039 Pharmacy
LA English
SL English
AB Nanospheres synthesized by salt-induced complex coacervation of cDNA and polycations such as gelatin and chitosan were evaluated as gene delivery vehicles. DNA-nanospheres in the size range of 200-750 nm could transfect a variety of cell lines. Although the transfection efficiency of the nanospheres was typically lower than that of lipofectamine and calcium phosphate controls in cell culture, the .beta.-gal expression in muscle of BALB/c mice was higher and more sustained than that achieved by naked DNA and lipofectamine complexes. This gene delivery system has several attractive features: (1) ligands can be conjugated to the nanosphere for targeting or stimulating receptor-mediated endocytosis; (2) lysosomolytic agents can be incorporated to reduce degradation of the DNA in the endosomal and lysosomal compartments; (3) other bioactive agents or multiple plasmids can be co- **encapsulated**; (4) bioavailability of the DNA can be improved because of protection from serum nuclease degradation by the polymeric matrix; (5) the nanosphere can be lyophilized for storage without loss of bioactivity.

L5 ANSWER 54 OF 87 CAPLUS COPYRIGHT 2003 ACS
AN 1998:672380 CAPLUS
DN 129:306500
TI Method of delivering a **lipid**-coated condensed-phase **microparticle** composition
IN Fernandez, Julio M.; Knudson, Mark B.
PA ACCESS Pharmaceuticals, Inc., USA
SO U.S., 37 pp., Cont.-in-part of U.S. Ser. No. 250,464.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5820879	A	19981013	US 1995-444244	19950518
	US 5654006	A	19970805	US 1994-250464	19940527
PRAI	US 1993-17681		19930212		
	US 1994-250464		19940527		
	WO 1994-US1924		19940210		

AB A method of delivering a therapeutic compd. to an in vivo target site having a selected pH, temp., ligand concn. or binding-mol. characteristic is disclosed. The method includes entrapping the therapeutic compd. in an **encapsulated microparticle** compn. that, when exposed to a selected target stimulus related to pH, temp., radiation, or the presence of a selected ligand or ion-channel activator, decondenses to release the compd. into the target site. The **encapsulated microparticle** compn. consists of a condensed-phase particle matrix contg. the compd. to be delivered in entrapped form, and a stimulus-responsive **lipid** bilayer membrane formed around the matrix. Localized perturbation of the **lipid** membrane, and influx of monovalent counterions into the polymer matrix, in response to the selected target stimulus, causes matrix swelling and compd. release from the particles.

L5 ANSWER 27 OF 87 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2001062270 EMBASE
TI Plasmid DNA **encapsulation** and release from solvent diffusion nanospheres.
AU Hirosue S.; Muller B.G.; Mulligan R.C.; Langer R.
CS R. Langer, Harvard-MIT Joint Program, Massachusetts Inst. of Technology, 45 Carleton Street, Cambridge, MA 02139, United States
SO Journal of Controlled Release, (29 Jan 2001) 70/1-2 (231-242).
Refs: 50
ISSN: 0168-3659 CODEN: JCREEC
PUI S 0168-3659(00)00353-9
CY Netherlands
DT Journal; Article
FS 022 Human Genetics
037 Drug Literature Index
039 Pharmacy
LA English
SL English
AB The first step toward hydrophobic polymer-based nanospheres for gene delivery is to **encapsulate** and release plasmid DNA. However, **encapsulating** large hydrophilic molecules in very small nanospheres has been difficult, and only a few examples exist in the literature. For example, maximizing protein and peptide as well as small molecule **encapsulation** requires adjustments in pH or addition of excipients to charge neutralize, and make less hydrophilic, the compound to be **encapsulated**. Following this model, we have used a cationic **lipid** to load and release plasmid DNA from nanospheres made by the phase inversion/solvent diffusion method. .COPYRGT. 2001 Elsevier Science B.V.

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L5 ANSWER 22 OF 87 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
AN 2002-10449 BIOTECHDS
TI **Microparticle** useful for the delivery of bioactive agent, e.g. nucleic acid comprises polymeric matrix, an anionic and zwitterionic **lipid** and nucleic acid molecule;
useful as a vector to deliver DNA, peptide and protein into animal tissue cell for e.g. gene therapy
AU BARMAN S P; MCKEEVER U; HEDLEY M L
PA ZYCOS INC
PI WO 2001093835 13 Dec 2001
AI WO 2000-US17971 2 Jun 2000
PRAI US 2000-208830 2 Jun 2000
DT Patent
LA English
OS WPI: 2002-188239 [24]
AB DERWENT ABSTRACT:
NOVELTY - A **microparticle** having diameter of less than 100 microns, comprising a polymeric matrix (a), a **lipid** (l1) having a pKa of less then 2.5 or a zwitterionic **lipid** (l2) and a nucleic acid molecule (c), is new. The **microparticle** is not **encapsulated** in a **liposome** and does not comprise a cell.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) preparation comprising the novel **microparticle**; (2) administering a nucleic acid to an animal by introducing the **microparticle** into the animal; and (3) preparing the **microparticle**, comprising: (a) providing a first solution containing (a) and (l1); (b) providing a second solution containing (c) dissolved or suspended in a solvent; (c) mixing the first and second to form a first emulsion; and (d) mixing the first emulsion with a third solution to form a second emulsion, where (3) and (4) are carried out in a manner that minimizes sharing of the nucleic acid while producing microparticles having an average diameter smaller than 100 microns.

USE - For delivering bioactive agent e.g. peptide, protein or nucleic acid into cells.

ADMINISTRATION - The **microparticle** is introduced into a mucosal tissue (preferably vaginal or rectal tissue) of the animal. The **microparticle** can be delivered orally, nasally, intralesionally, subcutaneously, intradermally or intramuscularly. No dosage is suggested.

ADVANTAGE - The **microparticle** is act as a highly effective vehicle for the delivery of bioactive agents into cells.

EXAMPLE - To prepare **lipid**-containing microparticles, poly-lactic-co-glycolic acid (PLGA) (200 mg) was dissolved in methylene chloride (DCM) (7 ml). The resulting PLGA/DCM solution was poured into a 35 ml polypropylene cylindrical tube. OVOTHIN (RTM) (**lipid** solution) was added to the PLGA/DCM solution to a final concentration of 0.05 % (vol/vol). Polyvinyl alcohol (PVA) (1 %; 50 ml) and 0.05 % PVA/300 Mm sucrose solution (100 ml) was poured into the above solution and homogenized. pBVKCMluc DNA (1.2 mg) in tris-HCl-EDTA (ethylenediaminetetraacetic acid)(TE)/10 % sodium dodecyl sulfate (SDS) (300 ml) was added to the PLGA/DCM solution. The mixture was homogenized for 2 minutes to form a DNA/PLGA emulsion. The DNA/PLGA emulsion was then immediately poured into 1% PVA solution and homogenized for 1 minutes. The mixture was then poured into the beaker containing 0.05 % PVA on the stir plate and stirred for two hours. The mixture was then centrifuged. The pelleted microparticles were washed twice with water. After second washing the pellet was resuspended in water, frozen in liquid nitrogen and lyophilized for at least 11 hours. DNA from microparticles prepared using TE/sucrose was present in a concentration of 2.33 micro-g/m (DNA/PLGA) and 55 % supercoiling, whereas DNA from microparticles

prepared using OVOTHIN (RTM) was present at a concentration of 1.66 micro-g/ml and 60 % supercoiling.(100 pages)

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US Pre-Grant Publication Full-Text Database
JPO Abstracts Database
EPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

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DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ			
L7	l5 and l4	1	L7
L6	L5 same l4	0	L6
L5	fusogenic	1248	L5
L4	L3 with l2 with l1	142	L4
L3	liposome or lipid or amphiphile	88902	L3
L2	encapsula$	153801	L2
L1	nanoparticle	4637	L1

END OF SEARCH HISTORY

L4: Entry 39 of 142 File: PGPB Sep 19, 2002

DOCUMENT-IDENTIFIER: US 20020131952 A1
TITLE: Hydrolysable hydrogels for controlled release

Summary of Invention Paragraph (48):
[0048] As indicated herein-above, the releasable compound can be a protein drug. However, it is also possible to encapsulate pharmacon containing nanoparticles, e.g. liposomes, iscoms, polylactic acid particles, polycaprolacton particles and gene delivery systems known to the person skilled in the art. The encapsulation of these nanoparticles has the advantage of preventing the occurence of a too fast release of the encapsulated compound, or, said in other words, burst-effects can be avoided in a more secure way.

DOCUMENT-IDENTIFIER: US 20020127224 A1
TITLE: Use of photoluminescent nanoparticles for photodynamic therapy

Detail Description Paragraph (44):
[0070] An alternate procedure for delivering nanoparticles to the treatment site involves encapsulating them in liposomes, microcapsules or nanocapsules, or other such drug carriers. Methods known to those in this field for incorporating small particles of a size similar to that of lightemitting nanoparticles can be utilized (see, e.g.; U.S. Pat. No. 5,686,113). Nanocapsules may be targeted to the treatment site by attachment of functional or delivery moieties on their outer surfaces as described above, such as antibodies or other delivery moieties. See also L. Cattel et al., "The role of conjugation processes and linking agents in the preparation of molecular/particulate conjugates--a review," S.T.P. Pharma Sciences 9 (4), pp. 307-319 (1999).